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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,729	04/30/2001	George Jackowski	2132.031	3806

21917 7590 03/11/2003

MCHALE & SLAVIN  
4440 PGA BLVD  
SUITE 402  
PALM BEACH GARDENS, FL 33410

EXAMINER
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COOK, LISA V

ART UNIT	PAPER NUMBER
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1641

14

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application N .

09/845,729

Applicant(s)

JACKOWSKI ET AL.

Examiner

Lisa V. Cook

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 February 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 1,2,10-17 and 29-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3-9,18-28 and 33-35 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-35 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9 & 12.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group II (claims 3-9, 18-28, and 33-35) in Paper No. 13 filed 2/5/03 is acknowledged. Applicant traverses the instant Restriction under Ochiai and further points to the office rejoining in related application no. 09/846,352 a prior to Allowance. Examiner acknowledges the in re Ochiai practice and will rejoin once allowable subject matter is determined.

In re Ochiai, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995) and In re Brouwer, 77 F.3d 422, 37 USPQ2d 1663 (Fed. Cir. 1996) addressed the issue of whether an otherwise conventional process could be patented if it were limited to making or using a nonobvious product. In both cases, the Federal Circuit held that the use of per se rules is improper in applying the test for obviousness under 35 U.S.C. 103. Rather, 35 U.S.C. 103 requires a highly fact-dependent analysis involving taking the claimed subject matter as a whole and comparing it to the prior art. To support a rejection under 35 U.S.C. 103, the collective teachings of the prior art must have suggested to one of ordinary skill in the art that, at the time the invention was made, applicant's claimed invention would have been obvious. In applying this test to the claims on appeal in Ochiai and Brouwer, the court held that there simply was no suggestion or motivation in the prior art to make or use novel, nonobvious products in the claimed processes. Consequently, the court overturned the rejections based upon 35 U.S.C. 103

The Restriction Requirement is deemed proper and is therefore made **FINAL**.

2. Claims 1-2, 10-17, and 29-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim. Currently claims 3-9, 18-28, and 33-35 are under consideration.

***Priority***

3. The instant application does not claim priority or benefits to an earlier application.

***Information Disclosure Statement***

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the Examiner on form PTO-892 or Applicant on form PTO-1449 has cited the references they have not been considered. With respect to the IDS filed 8/13/01 in paper #5 it is noted that the IDS is not found in the application. Applicant is invited to re-submit the IDS for consideration.
5. The information disclosure statements filed 2/14/02 in paper #9 and filed 12/9/02 in paper #12 have been considered as to the merits prior to first action.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 3-9, 18-28, and 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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A. In claims 3-5 the terms "evidencing" and "characterizing" are vague and indefinite because it is not clear as to what "evidencing" and "characterizing" encompasses. If the method merely detects myocardial infarction or renal failure via a biopolymer marker as (defined in the disclosure) it is suggested that the phrases are replaced with "detecting" in order to clarify applicant's intended meaning.

B. The term "regulation" in claim 35 is a relative term which renders the claim indefinite. The term "regulation" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear as to how the measurement of the biopolymer marker will further serve to control the absence and/or presence of the aforementioned biopolymer or an analyte thereof. It is suggested that the claim merely recite detection of the biopolymer.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 3-9, 18-28, and 33-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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Claims 3-9, 18-28, and 33-35 are broadly drawn to methods of determining the presence or absence of myocardial infarction or renal failure by analyzing a biological sample obtained from a patient to identify the biopolymer marker sequence consisting of sequence identification N0:1. The specification also contemplates the use of these methods for diagnosing, staging, monitoring, prognosticating or determining predisposition to myocardial infarction or renal failure. These diagnostic methods include for example biopolymer evidencing, characterization, regulation, risk-assessment, and therapeutic identification.

The specification asserts that the said target sequence was found in myocardial infarction or renal disease. However, the obtained results set forth in the specification for example in figure 1 is not clearly indicative of myocardial infarction and renal disease, because no control sample analysis is presented by way of example. Further it is not clear how the same biopolymer marker will be utilized to distinguish the two unrelated disease states. In other words how will one identify myocardial infarction from renal failure. The specification does not enable one of ordinary skill in the art to definitively assess the incidence or further distinguish between both diseases in a single test sample. And while the evidence presented in the specification does point to the high occurrence of the sequence in both myocardial infarction and renal disease, this is not sufficient in implementing the said sequences in a molecular based diagnostic method for both myocardial infarction and renal disease with the said sequence. Furthermore, Applicants have not provided any disclosure enabling the use of the biopolymer marker with regard to regulating the presence or absence of said sequence. There is no disclosure designating how the sequence bound in the method that could be regarded as enabling one of ordinary skill in the art to use the said sequences in the diagnostic method.

Applicants have not set forth any supporting evidence that suggests that any of the sequences (SEQ ID NO: 1) are unique molecular markers for myocardial infarction or renal failure. Tascilar et al. (Annals of Oncology 10, Suppl. 4: S107-S110, 1999) reports on diagnostic methods in the realm of disease states, however this review article is relevant to Applicants' claimed invention. It is art known that molecular-based assays are valid tools used in predicting and detecting diseases, however as assessed in the Tascilar review "...these tests should be interpreted with caution..." and "the genetic changes found in sources other than the pancreas itself (blood, stool) should be evaluated prudently".

Furthermore, Tockman et al. (Cancer Research 52: 2711s-2718s, 1992) teach considerations necessary for a suspected cancer biomarker (intermediate end point marker) to have efficacy and success in a clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly applicable to other oncogenic disorders. Tockman teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials, see abstract. Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and **if validated** (emphasis added) can be used for population screening (p. 2713s, column 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome.

The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. “This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point [marker]”, see page 2714s, column 1, Biomarker Validation against Acknowledged Disease End Points section. Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials, see page 2716s, column 2, Summary section. Tockman reiterates that the predictability of the art in regards to cancer prognosis and the estimation of life expectancies within a population with a disease or disorder is highly speculative and unpredictable.

Based on the analysis and the teachings presented above it would require undue experimentation for the skilled artisan to practice this invention because there is no support in the specification for the enablement of the broadly claimed invention. Therefore, in view of the insufficient guidance in the specification, extensive experimentation would be required to enable the claims and to practice the invention as claimed.

11. Claims ~~309~~, 18-28, and 33-35 are free of the art.
12. For reasons aforementioned, no claims are allowed.



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13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



*Lisa V. Cook*

CM1-7B17

(703) 305-0808

3/7/03



LONG V. LE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600

03/10/03